Full Title: Phase III Study of Radiation Therapy with or without Temozolomide for Symptomatic or Progressive Low-Grade Gliomas

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Objectives: The primary aim of this trial is to determine whether the addition of temozolomide to fractionated radiotherapy improves the progression-free survival (PFS) of patients requiring treatment for low-grade gliomas. Survival based on 1p and 19q deletion status will be assessed. Toxicity, quality of life, and cognitive effects will also be evaluated.

Eligibility:

1. Age ≥ 18 years.
2. Tumors must be supratentorially located.
3. Pathological diagnosis of astrocytoma grade 2, oligodendroglioma grade 2, or oligoastrocytoma grade 2 (mixed glioma containing astrocytoma and oligodendroglioma). Pilocytic astrocytoma, ganglioglioma, pleomorphic xanthoastrocytoma, or dysembryoplastic neuroepithelial tumors are not eligible. NOTE: If the pathology from multiple procedures supports the diagnosis of a brain tumor, the qualifying pathology of grade 2 astrocytoma, oligodendroglioma, or oligoastrocytoma must be the most recent pathological diagnosis, and a pathological diagnosis of a grade 3 or grade 4 glioma must not have been made at any time.
4. Patients must have paraffin-embedded tumor specimen available for submission for confirmation of pathological diagnosis and determination of 1p/19q deletion status. NOTE: It is recommended that patients not be Pre-registered until the required tumor specimens are on hand and ready for submission as outlined in Section 10. If submission of tissue will be submitted more than 5 working days after pre-registration, immediately notify the Mayo Clinic Cytogenetics Laboratory via email: ecog.E3F05_TISSUE@jimmy.harvard.edu
5. The patient must currently have at least one of the following:
   - Uncontrolled symptoms, defined as any of the below:
     - Headaches associated with mass effect
     - Uncontrolled seizures despite 2 different antiepileptic drug regimens (i.e., 2 antiepileptic drugs tested either sequentially or in combination)
     - Focal neurological symptoms
     - Cognitive symptoms or deficits
   OR
   - Tumor progression by serial MRIs, defined as any of the below:
     - New or progressive enhancement
     - New or progressive T2 or FLAIR signal abnormality
   OR
   - Age ≥ 40 years. NOTE: Patients aged less than 40 whose only symptom of low-grade glioma is seizures that are well-controlled on antiepileptic drugs, and who have no evidence of radiographic progression, are ineligible. The rationale is that such patients have a relatively good prognosis and are often managed expectantly with observation. Excluding such patients will maintain similar eligibility requirements with the ongoing EORTC trial comparing radiation to temozolomide for patients with low-grade gliomas.

5. Patient must be able to undergo MRI with and without contrast. Patients who are unable to undergo MRI are ineligible.

6. MRI and chest x-ray within 6 weeks prior to pre-registration. If resection was performed, MRI after surgery is required.

7. No previous radiation, cytotoxic chemotherapy, radio surgery, or investigational treatment directed at the brain tumor at any time. No limit on number of previous surgical procedures of this tumor.

8. No previous radiation treatment to the head (unless the ports for that radiation entirely excluded the brain) for any condition.

9. Karnofsky performance status ≥ 60%.

10. No other diagnosed malignancy (except non-melanoma skin cancer or cervical carcinoma in situ, which are allowable), unless the patient has been disease-free for at least 5 years.

11. No medical disorder that increases risks of radiation or TMZ chemotherapy. No uncontrolled infection. No known positivity for human immunodeficiency virus (HIV), as temozolomide is known to cause immunosuppression and increase risk of opportunistic infection. No other disorder limiting expected survival to < 5 years.
12. Patients who have undergone gross total resection and have no detectable residual disease are eligible.

Randomization (Step 1)

1. Eligibility per pathologic diagnosis confirmed by central review and 1p/19q deletion status assessment have been received from the central reviewers.

2. Must be able to start treatment with RT within 2 weeks or 10 working days at a qualified center (to be defined by the Radiation Oncology chair) and to start TMZ prescribed at a participating center within 2 weeks or 10 working days of randomization.

3. CBC requirements within 14 days prior to randomization:
   - White blood count (WBC) ≥ 3,000 /mm³
   - Absolute neutrophil count (ANC) ≥ 1,500 /mm³
   - Platelets ≥ 100,000 /mm³
   - Hematocrit ≥ 30%

4. Chemistry requirements within 14 days prior to randomization:
   - Bilirubin ≤ 2 x upper limit of normal (ULN)
   - AST ≤ 3 x ULN (SGOT)
   - Creatinine ≤ 2.0 x ULN
   - ALT ≤ 3 x ULN (SGPT)

5. Women must not be pregnant or breast-feeding due to known and potential teratogenic effects of radiotherapy and temozolomide and the uncertain safety of temozolomide in lactation. All females of childbearing potential must have a blood test or urine study within 2 weeks prior to randomization to rule out pregnancy.

6. Women of childbearing potential and sexually active males are strongly advised to use an accepted and effective method of contraception.

7. Patient must be at least two weeks post any brain surgery at the time of randomization.

EXCLUSION CRITERIA

Exclusion Criteria Not Available